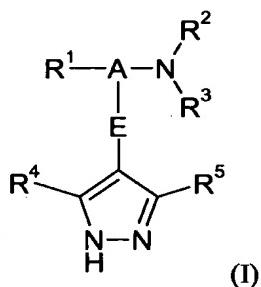


**CLAIMS**

1. A compound of the formula (I):



or a salt, solvate, tautomer or N-oxide thereof;

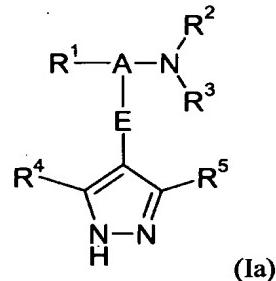
- 5       wherein A is a saturated hydrocarbon linker group containing from 1 to 7 carbon atoms, the linker group having a maximum chain length of 5 atoms extending between R<sup>1</sup> and NR<sup>2</sup>R<sup>3</sup> and a maximum chain length of 4 atoms extending between E and NR<sup>2</sup>R<sup>3</sup>, wherein one of the carbon atoms in the linker group may optionally be replaced by an oxygen or nitrogen atom; and wherein the carbon atoms of the linker group A may optionally bear one or more substituents selected from oxo, fluorine and hydroxy, provided that the hydroxy group when present is not located at a carbon atom  $\alpha$  with respect to the NR<sup>2</sup>R<sup>3</sup> group and provided that the oxo group when present is located at a carbon atom  $\alpha$  with respect to the NR<sup>2</sup>R<sup>3</sup> group;
- 10      E is a monocyclic or bicyclic carbocyclic or heterocyclic group wherein E is unsubstituted or has up to 4 substituents R<sup>8</sup> selected from hydroxy, oxo (when E is non-aromatic), chlorine, bromine, trifluoromethyl, cyano, C<sub>1-4</sub> hydrocarbyloxy and C<sub>1-4</sub> hydrocarbyl optionally substituted by C<sub>1-2</sub> alkoxy or hydroxyl;
- 15      R<sup>1</sup> is an aryl or heteroaryl group which is unsubstituted or bears one or more substituents selected from hydroxy; C<sub>1-4</sub> acyloxy; fluorine; chlorine; bromine; trifluoromethyl; cyano; CONH<sub>2</sub>; nitro; C<sub>1-4</sub> hydrocarbyloxy and C<sub>1-4</sub> hydrocarbyl each optionally substituted by C<sub>1-2</sub> alkoxy, carboxy or hydroxy; C<sub>1-4</sub>

- acylamino; benzoylamino; pyrrolidinocarbonyl; piperidinocarbonyl; morpholinocarbonyl; piperazinocarbonyl; five and six membered heteroaryl and heteroaryloxy groups containing one or two heteroatoms selected from N, O and S; phenyl; phenyl-C<sub>1-4</sub> alkyl; phenyl-C<sub>1-4</sub> alkoxy; heteroaryl-C<sub>1-4</sub> alkyl; heteroaryl-C<sub>1-4</sub> alkoxy and phenoxy, wherein the heteroaryl, heteroaryloxy, phenyl, phenyl-C<sub>1-4</sub> alkyl, phenyl-C<sub>1-4</sub> alkoxy, heteroaryl-C<sub>1-4</sub> alkyl, heteroaryl-C<sub>1-4</sub> alkoxy and phenoxy groups are each optionally substituted with 1, 2 or 3 substituents selected from C<sub>1-2</sub> acyloxy, fluorine, chlorine, bromine, trifluoromethyl, cyano, CONH<sub>2</sub>, C<sub>1-2</sub> hydrocarbyloxy and C<sub>1-2</sub> hydrocarbyl each optionally substituted by methoxy or hydroxyl;
- R<sup>2</sup> and R<sup>3</sup> are independently selected from hydrogen, C<sub>1-4</sub> hydrocarbyl and C<sub>1-4</sub> acyl wherein the hydrocarbyl and acyl moieties are optionally substituted by one or more substituents selected from fluorine, hydroxy, amino, methylamino, dimethylamino and methoxy;
- 15        or R<sup>2</sup> and R<sup>3</sup> together with the nitrogen atom to which they are attached form a cyclic group selected from an imidazole group and a saturated monocyclic heterocyclic group having 4-7 ring members and optionally containing a second heteroatom ring member selected from O and N;
- or one of R<sup>2</sup> and R<sup>3</sup> together with the nitrogen atom to which they are attached and one or more atoms from the linker group A form a saturated monocyclic heterocyclic group having 4-7 ring members and optionally containing a second heteroatom ring member selected from O and N;
- 20        or NR<sup>2</sup>R<sup>3</sup> and the carbon atom of linker group A to which it is attached together form a cyano group;
- 25        R<sup>4</sup> is selected from hydrogen, halogen, C<sub>1-5</sub> saturated hydrocarbyl, C<sub>1-5</sub> saturated hydrocarbyloxy, cyano, and CF<sub>3</sub>; and
- R<sup>5</sup> is selected from hydrogen, halogen, C<sub>1-5</sub> saturated hydrocarbyl, C<sub>1-5</sub> saturated hydrocarbyloxy, cyano, CONH<sub>2</sub>, CONHR<sup>9</sup>, CF<sub>3</sub>, NH<sub>2</sub>, NHCOR<sup>9</sup> or NHCONHR<sup>9</sup>;

$R^9$  is a group  $R^{9a}$  or  $(CH_2)R^{9a}$ , wherein  $R^{9a}$  is a monocyclic or bicyclic group which may be carbocyclic or heterocyclic;

- the carbocyclic group or heterocyclic group  $R^{9a}$  being optionally substituted by one or more substituents selected from halogen, hydroxy, trifluoromethyl, cyano, nitro, carboxy, amino, mono- or di- $C_{1-4}$  hydrocarbyl amino; a group  $R^a\text{-}R^b$  wherein  $R^a$  is a bond, O, CO,  $X^1C(X^2)$ ,  $C(X^2)X^1$ ,  $X^1C(X^2)X^1$ , S, SO,  $SO_2$ ,  $NR^c$ ,  $SO_2NR^c$  or  $NR^cSO_2$ ; and  $R^b$  is selected from hydrogen, heterocyclic groups having from 3 to 12 ring members, and a  $C_{1-8}$  hydrocarbyl group optionally substituted by one or more substituents selected from hydroxy, oxo, halogen, cyano, nitro, carboxy, amino, mono- or di- $C_{1-4}$  hydrocarbyl amino, carbocyclic and heterocyclic groups having from 3 to 12 ring members and wherein one or more carbon atoms of the  $C_{1-8}$  hydrocarbyl group may optionally be replaced by O, S, SO,  $SO_2$ ,  $NR^c$ ,  $X^1C(X^2)$ ,  $C(X^2)X^1$  or  $X^1C(X^2)X^1$ ;
- $R^c$  is selected from hydrogen and  $C_{1-4}$  hydrocarbyl; and  $X^1$  is O, S or  $NR^c$  and  $X^2$  is =O, =S or = $NR^c$ ;
- but excluding the compound (2R, 5S)-1-benzyl-4-(R)-1-(3-[1-(tert-butyl)-1,1-dimethylsilyl]oxyphenyl)-1-[4-(1H-pyrazol-4-yl)phenyl]methyl-2,5-dimethylhexahdropyrazine.

- 20 2. A compound according to claim 1 of the formula (Ia):



or a salt, solvate, tautomer or N-oxide thereof;

wherein A is a saturated hydrocarbon linker group containing from 1 to 7 carbon atoms, the linker group having a maximum chain length of 5 atoms extending between R<sup>1</sup> and NR<sup>2</sup>R<sup>3</sup> and a maximum chain length of 4 atoms extending between E and NR<sup>2</sup>R<sup>3</sup>, wherein one of the carbon atoms in the linker group may optionally be replaced by an oxygen or nitrogen atom; and wherein the carbon atoms of the linker group A may optionally bear one or more substituents selected from oxo, fluorine and hydroxy, provided that the hydroxy group when present is not located at a carbon atom  $\alpha$  with respect to the NR<sup>2</sup>R<sup>3</sup> group and provided that the oxo group when present is located at a carbon atom  $\alpha$  with respect to the NR<sup>2</sup>R<sup>3</sup> group;

5 E is a monocyclic or bicyclic carbocyclic or heterocyclic group wherein E is unsubstituted or has up to 4 substituents R<sup>8</sup> as defined in claim 1;

10 R<sup>1</sup> is an aryl or heteroaryl group which is unsubstituted or substituted as defined in claim 1

15 R<sup>2</sup> and R<sup>3</sup> are independently selected from hydrogen, C<sub>1-4</sub> hydrocarbyl and C<sub>1-4</sub> acyl;

or R<sup>2</sup> and R<sup>3</sup> together with the nitrogen atom to which they are attached form a saturated monocyclic heterocyclic group having 4-7 ring members and optionally containing a second heteroatom ring member selected from O and N;

20 or one of R<sup>2</sup> and R<sup>3</sup> together with the nitrogen atom to which they are attached and one or more atoms from the linker group A form a saturated monocyclic heterocyclic group having 4-7 ring members and optionally containing a second heteroatom ring member selected from O and N;

25 or NR<sup>2</sup>R<sup>3</sup> and the carbon atom of linker group A to which it is attached together form a cyano group;

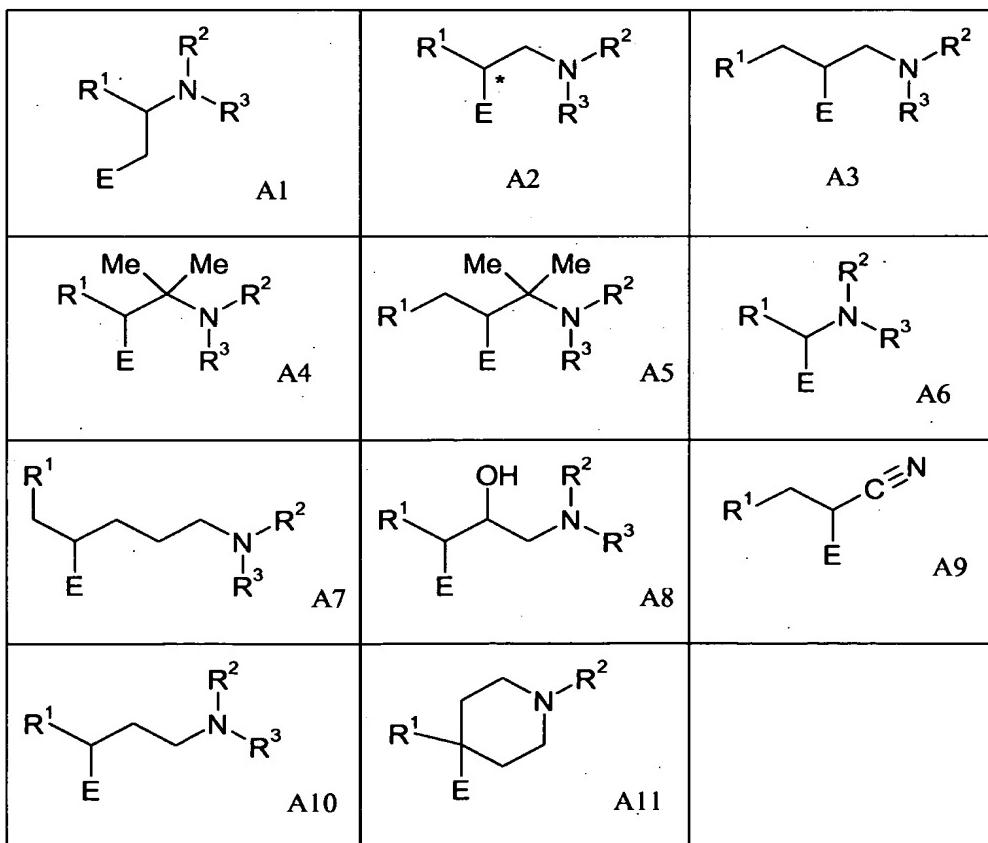
R<sup>4</sup> is selected from hydrogen, halogen, C<sub>1-5</sub> saturated hydrocarbyl, cyano and CF<sub>3</sub>; and

R<sup>5</sup> is selected from hydrogen, halogen, C<sub>1-5</sub> saturated hydrocarbyl, cyano, CONH<sub>2</sub>, CONHR<sup>9</sup>, CF<sub>3</sub>, NH<sub>2</sub>, NHCOR<sup>9</sup> or NHCONHR<sup>9</sup>;

- $R^9$  is phenyl or benzyl each optionally substituted by one or more substituents selected from halogen, hydroxy, trifluoromethyl, cyano, nitro, carboxy, amino, mono- or di- $C_{1-4}$  hydrocarbyl amino; a group  $R^a\text{-}R^b$  wherein  $R^a$  is a bond, O, CO,  $X^1C(X^2)$ ,  $C(X^2)X^1$ ,  $X^1C(X^2)X^1$ , S, SO,  $SO_2$ ,  $NR^c$ ,  $SO_2NR^c$  or  $NR^cSO_2$ ; and  $R^b$  is selected from hydrogen, heterocyclic groups having from 3 to 12 ring members, and a  $C_{1-8}$  hydrocarbyl group optionally substituted by one or more substituents selected from hydroxy, oxo, halogen, cyano, nitro, carboxy, amino, mono- or di- $C_{1-4}$  hydrocarbyl amino, carbocyclic and heterocyclic groups having from 3 to 12 ring members and wherein one or more carbon atoms of the  $C_{1-8}$  hydrocarbyl group may optionally be replaced by O, S, SO,  $SO_2$ ,  $NR^c$ ,  $X^1C(X^2)$ ,  $C(X^2)X^1$  or  $X^1C(X^2)X^1$ ;
- $R^c$  is selected from hydrogen and  $C_{1-4}$  hydrocarbyl; and
- $X^1$  is O, S or  $NR^c$  and  $X^2$  is =O, =S or = $NR^c$ ;
- but excluding the compound (2R, 5S)-1-benzyl-4-(R)-1-(3-[1-(tert-butyl)-1,1-dimethylsilyloxyphenyl]-1-[4-(1H-pyrazol-4-yl)phenyl]methyl-2,5-dimethylhexahdropyrazine.
3. A compound according to claim 1 or claim 2 wherein A is a saturated hydrocarbon linker group containing from 1 to 7 carbon atoms, the linker group having a maximum chain length of 5 atoms extending between  $R^1$  and  $NR^2R^3$  and a maximum chain length of 4 atoms extending between E and  $NR^2R^3$ , wherein one of the carbon atoms in the linker group may optionally be replaced by an oxygen or nitrogen atom; and wherein the carbon atoms of the linker group A may optionally bear one or more substituents selected from fluorine and hydroxy, provided that the hydroxy group when present is not located at a carbon atom  $\alpha$  with respect to the  $NR^2R^3$  group; and
- $R^5$  is selected from selected from hydrogen, halogen,  $C_{1-5}$  saturated hydrocarbyl, cyano,  $CONH_2$ ,  $CF_3$ ,  $NH_2$ ,  $NHCOR^9$  and  $NHCONHR^9$ .
4. A compound according to any one of claims 1 to 3 wherein the linker group A has a maximum chain length of 3 atoms extending between  $R^1$  and  $NR^2R^3$ .

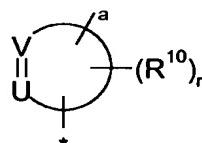
5. A compound according to claim 4 wherein the linker group A has a maximum chain length of 2 atoms extending between R<sup>1</sup> and NR<sup>2</sup>R<sup>3</sup>.
6. A compound according to any one of claims 1 to 5 wherein the linker group A has a maximum chain length of 3 atoms extending between E and NR<sup>2</sup>R<sup>3</sup>.
- 5 7. A compound according to claim 6 wherein the linker group A has a chain length of 2 or 3 atoms extending between R<sup>1</sup> and NR<sup>2</sup>R<sup>3</sup> and a chain length of 2 or 3 atoms extending between E and NR<sup>2</sup>R<sup>3</sup>.
8. A compound according to any one of the preceding claims wherein the linker group atom linked directly to the group E is a carbon atom and the linker group A has an all-carbon skeleton.
- 10 9. A compound according to any one of claims 1 to 7 wherein the portion R<sup>1</sup>-A-NR<sup>2</sup>R<sup>3</sup> of the compound is represented by the formula R<sup>1</sup>-(G)<sub>k</sub>-(CH<sub>2</sub>)<sub>m</sub>-W-O<sub>b</sub>-(CH<sub>2</sub>)<sub>n</sub>-(CR<sup>6</sup>R<sup>7</sup>)<sub>p</sub>-NR<sup>2</sup>R<sup>3</sup> wherein G is NH, NMe or O; W is attached to the group E and is selected from (CH<sub>2</sub>)<sub>j</sub>-CR<sup>20</sup>, (CH<sub>2</sub>)<sub>j</sub>-N and (NH)<sub>j</sub>-CH; b is 0 or 1, j is 0 or 1, k is 0 or 1, m is 0 or 1, n is 0, 1, 2, or 3 and p is 0 or 1; the sum of b and k is 0 or 1; the sum of j, k, m, n and p does not exceed 4; R<sup>6</sup> and R<sup>7</sup> are the same or different and are selected from methyl and ethyl, or CR<sup>6</sup>R<sup>7</sup> forms a cyclopropyl group; and R<sup>20</sup> is selected from hydrogen, methyl, hydroxy and fluorine.
- 15 10. A compound according to any one of claims 1 to 7 wherein the moiety R<sup>1</sup>-A-NR<sup>2</sup>R<sup>3</sup> is represented by the formula R<sup>1</sup>-(G)<sub>k</sub>-(CH<sub>2</sub>)<sub>m</sub>-X-(CH<sub>2</sub>)<sub>n</sub>-(CR<sup>6</sup>R<sup>7</sup>)<sub>p</sub>-NR<sup>2</sup>R<sup>3</sup> wherein G is NH, NMe or O; X is attached to the group E and is selected from (CH<sub>2</sub>)<sub>j</sub>-CH, (CH<sub>2</sub>)<sub>j</sub>-N and (NH)<sub>j</sub>-CH; j is 0 or 1, k is 0 or 1, m is 0 or 1, n is 0, 1, 2, or 3 and p is 0 or 1, and the sum of j, k, m, n and p does not exceed 4; and R<sup>6</sup> and R<sup>7</sup> are the same or different and are selected from methyl and ethyl, or CR<sup>6</sup>R<sup>7</sup> forms a cyclopropyl group.
- 20 25 11. A compound according to claim 10 wherein (i) k is 0, m is 0 or 1, n is 0, 1, 2 or 3 and p is 0; or (ii) k is 0, m is 0 or 1, n is 0, 1 or 2 and p is 1.

12. A compound according to claim 10 wherein (i) X is  $(CH_2)_j\text{-CH}$ , k is 1, m is 0, n is 0, 1,2 or 3 and p is 0; or (ii) X is  $(CH_2)_j\text{-CH}$ , k is 1, m is 0, n is 0, 1 or 2 and p is 1.
13. A compound according to claim 10 or claim 12 wherein (i) j is 0; or (ii) j is 1; or (iii)  $\text{CR}^6\text{R}^7$  is  $\text{C}(\text{CH}_3)_2$ .
- 5 14. A compound according to claim 10 wherein the portion  $\text{R}^1\text{-A-NR}^2\text{R}^3$  of the compound is represented by the formula  $\text{R}^1\text{-X-(CH}_2\text{)}_n\text{-NR}^2\text{R}^3$  where X is attached to the group E and is a group CH, and n is 2.
15. A compound according to claim 1 or claim 2 wherein  $\text{R}^1\text{-A(E)-NR}^2\text{R}^3$  is selected from the groups A1 to A11 below:



16. A compound according to any one of the preceding claims wherein E is a monocyclic group.
17. A compound according to any one of the preceding claims wherein E is an aryl or heteroaryl group each of which is unsubstituted or substituted by up to 4 substituents R<sup>8</sup> as defined in claim 1.  
5
18. A compound according to claim 17 selected from optionally substituted phenyl, thiophene, furan, pyrimidine and pyridine groups, each of which is unsubstituted or substituted by up to 4 substituents R<sup>8</sup> as defined in claim 1.
19. A compound according to claim 18 wherein E is a phenyl group which is unsubstituted or substituted by up to 4 substituents R<sup>8</sup> as defined in claim 1.  
10
20. A compound according to any one of the preceding claims wherein the group A and the pyrazole group are attached to the group E in a *meta* or *para* relative orientation; i.e. A and the pyrazole group are not attached to adjacent ring members of the group E.
- 15 21. A compound according to claim 20 wherein E is selected from 1,4-phenylene, 1,3-phenylene, 2,5-pyridylene and 2,4-pyridylene, 1,4-piperazinyl, and 1,4-piperazonyl, each of which is unsubstituted or substituted by up to 4 substituents R<sup>8</sup> as defined in claim 1.
22. A compound according to any one of the preceding claims wherein E has 0-3  
20 substituents.
23. A compound according to claim 22 wherein E has 0-2 substituents
24. A compound according to claim 23 wherein E has 0 or 1 substituent.
25. A compound according to claim 24 wherein E is unsubstituted.

26. A compound according to any one of the preceding claims wherein the group E is an aryl or heteroaryl group having five or six members and containing up to three heteroatoms selected from O, N and S, the group E being represented by the formula:



5

where \* denotes the point of attachment to the pyrazole group, and "a" denotes the attachment of the group A;

r is 0, 1 or 2;

U is selected from N and CR<sup>12a</sup>; and

10 V is selected from N and CR<sup>12b</sup>; where R<sup>12a</sup> and R<sup>12b</sup> are the same or different and each is hydrogen or a substituent containing up to ten atoms selected from C, N, O, F, Cl and S provided that the total number of non-hydrogen atoms present in R<sup>12a</sup> and R<sup>12b</sup> together does not exceed ten;

15 or R<sup>12a</sup> and R<sup>12b</sup> together with the carbon atoms to which they are attached form an unsubstituted five or six membered saturated or unsaturated ring containing up to two heteroatoms selected from O and N; and

R<sup>10</sup> is selected from halogen, hydroxy, trifluoromethyl, cyano, nitro, carboxy, amino, mono- or di-C<sub>1-4</sub> hydrocarbyl amino, carbocyclic and heterocyclic groups having from 3 to 12 ring members; a group R<sup>a</sup>-R<sup>b</sup> wherein R<sup>a</sup> is a bond, O, CO, X<sup>1</sup>C(X<sup>2</sup>), C(X<sup>2</sup>)X<sup>1</sup>, X<sup>1</sup>C(X<sup>2</sup>)X<sup>1</sup>, S, SO, SO<sub>2</sub>, NR<sup>c</sup>, SO<sub>2</sub>NR<sup>c</sup> or NR<sup>c</sup>SO<sub>2</sub>; and R<sup>b</sup> is selected from hydrogen, carbocyclic and heterocyclic groups having from 3 to 12 ring members, and a C<sub>1-8</sub> hydrocarbyl group optionally substituted by one or more substituents selected from hydroxy, oxo, halogen, cyano, nitro, carboxy, amino, mono- or di-C<sub>1-4</sub> hydrocarbyl amino, carbocyclic and heterocyclic groups having from 3 to 12 ring members and wherein one or more carbon atoms of the C<sub>1-8</sub>

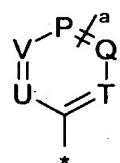
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hydrocarbyl group may optionally be replaced by O, S, SO, SO<sub>2</sub>, NR<sup>c</sup>, X<sup>1</sup>C(X<sup>2</sup>), C(X<sup>2</sup>)X<sup>1</sup> or X<sup>1</sup>C(X<sup>2</sup>)X<sup>1</sup>;

R<sup>c</sup> is selected from hydrogen and C<sub>1-4</sub> hydrocarbyl; and

X<sup>1</sup> is O, S or NR<sup>c</sup> and X<sup>2</sup> is =O, =S or =NR<sup>c</sup>.

- 5 27. A compound according to claim 26 wherein E is represented by the formula:



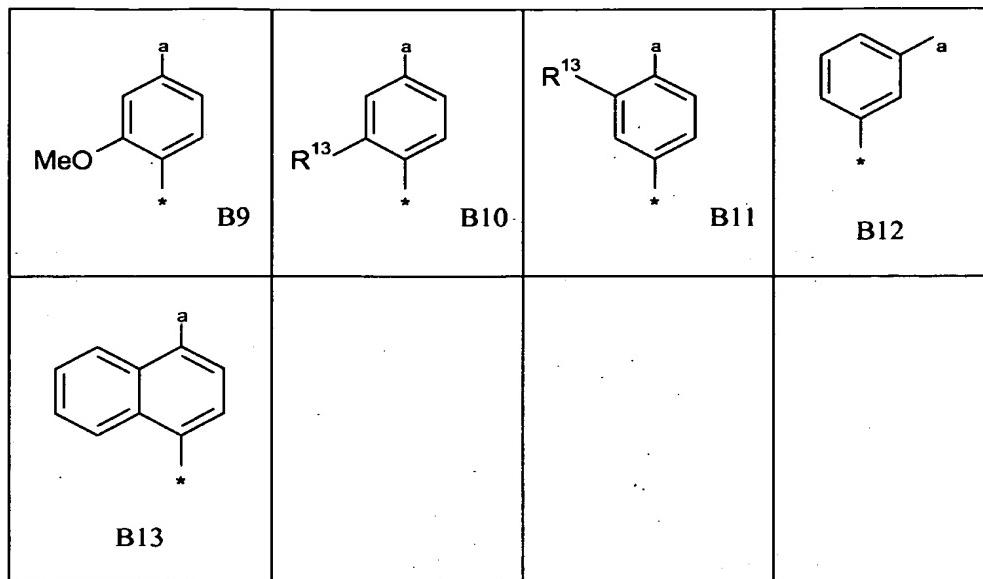
where P, Q and T are the same or different and are selected from N, CH and NCR<sup>10</sup>, provided that the group A is attached to a carbon atom.

28. A compound according to claim 27 wherein the group E is selected from groups  
10 B1 to B13 in the Table below:

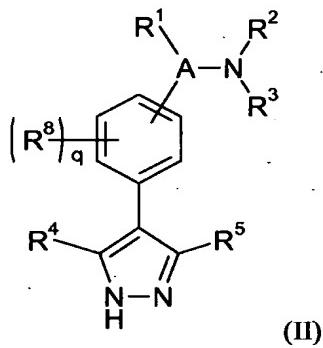
B1	B2	B3	B4

B5	B6	B7	B8



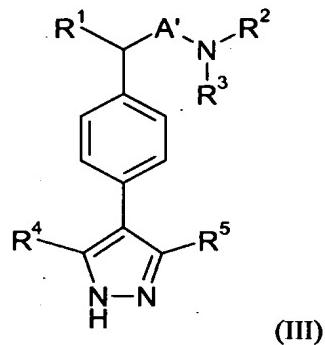
29. A compound according to claim 19 having the formula (II):



5       wherein the group A is attached to the *meta* or *para* position of the benzene ring  
 and q is 0-4; R<sup>8</sup> is hydroxy; halogen; trifluoromethyl; cyano; C<sub>1-4</sub> hydrocarbyloxy  
 optionally substituted by C<sub>1-2</sub> alkoxy or hydroxy; and C<sub>1-4</sub> hydrocarbyl optionally  
 substituted by C<sub>1-2</sub> alkoxy or hydroxy.

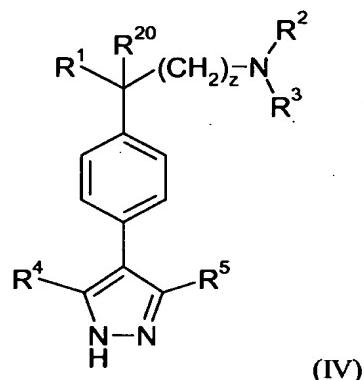
30. A compound according to claim 29 wherein q is 0, 1 or 2
31. A compound according to claim 30 wherein q is 0 or 1.

32. A compound according to claim 31 wherein q is 0.
33. A compound according to claim 19 having the formula (III):



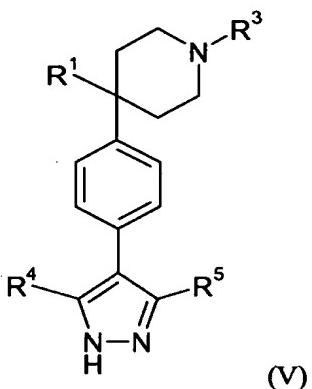
5 where A' is the residue of the group A and R<sup>1</sup> to R<sup>5</sup> are as defined in any one of  
the preceding claims.

34. A compound according to claim 19 having the formula (IV):



wherein z is 0, 1 or 2, R<sup>20</sup> is selected from hydrogen, methyl, hydroxy and fluorine, provided that when z is 0, R<sup>20</sup> is other than hydroxy.

- 10 35. A compound according to claim 19 having the formula (V):



wherein R<sup>3</sup> is optionally selected from hydrogen and C<sub>1-4</sub> hydrocarbyl.

- 36. A compound according to claim 35 wherein R<sup>3</sup> is selected from hydrogen and C<sub>1-4</sub> hydrocarbyl.
- 5    37. A compound according to claim 29 wherein R<sup>1</sup> is phenyl.
- 38. A compound according to any one of the preceding claims wherein R<sup>1</sup> is selected from phenyl, naphthyl, thieryl, furan, pyrimidine and pyridine, each optionally substituted as defined in claim 1.
- 39. A compound according to any one of the preceding claims wherein R<sup>1</sup> is
- 10    unsubstituted or is substituted by up to 5 substituents selected from hydroxy; C<sub>1-4</sub> acyloxy; fluorine; chlorine; bromine; trifluoromethyl; cyano; C<sub>1-4</sub> hydrocarbyloxy and C<sub>1-4</sub> hydrocarbyl optionally substituted by C<sub>1-2</sub> alkoxy or hydroxy; and five membered heteroaryl groups containing one or two heteroatoms selected from N, O and S, the heteroaryl groups being optionally substituted by one or more C<sub>1-4</sub> alkyl substituents.
- 15    40. A compound according to claim 23 wherein R<sup>1</sup> is unsubstituted or is substituted by up to 5 substituents selected from hydroxy, C<sub>1-4</sub> acyloxy, fluorine, chlorine, bromine, trifluoromethyl, cyano, C<sub>1-4</sub> hydrocarbyloxy and C<sub>1-4</sub> hydrocarbyl optionally substituted by C<sub>1-2</sub> alkoxy or hydroxy.

41. A compound according to claim 23 or 24 wherein the group R<sup>1</sup> has one or two substituents selected from fluorine, chlorine, trifluoromethyl, methyl and methoxy.
42. A compound according to claim 25 wherein R<sup>1</sup> is a mono-chlorophenyl or dichlorophenyl group.
43. A compound according to any one of the preceding claims wherein R<sup>4</sup> is selected from hydrogen and methyl.
44. A compound according to any one of the preceding claims wherein R<sup>5</sup> is selected from hydrogen, fluorine, chlorine, bromine, methyl, ethyl, hydroxyethyl, methoxymethyl, cyano, CF<sub>3</sub>, NH<sub>2</sub>, NHCOR<sup>9b</sup> and NHCONHR<sup>9b</sup> where R<sup>9b</sup> is phenyl or benzyl optionally substituted by hydroxy, C<sub>1-4</sub> acyloxy, fluorine, chlorine, bromine, trifluoromethyl, cyano, C<sub>1-4</sub> hydrocarbyloxy and C<sub>1-4</sub> hydrocarbyl optionally substituted by C<sub>1-2</sub> alkoxy or hydroxy.
45. A compound according to any one of the preceding claims wherein R<sup>2</sup> and R<sup>3</sup> are independently selected from hydrogen, C<sub>1-4</sub> hydrocarbyl and C<sub>1-4</sub> acyl
46. A compound according to claim 28 wherein R<sup>2</sup> and R<sup>3</sup> are independently selected from hydrogen and methyl.
47. A compound according to claim 29 wherein R<sup>2</sup> and R<sup>3</sup> are both hydrogen.
48. A compound according to any one of the preceding claims having a molecular weight of less than 525.
49. A compound according to claim 1 of the formula (I) which is:  
2-phenyl-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethylamine;  
3-phenyl-2-[3-(1H-pyrazol-4-yl)-phenyl]-propionitrile;  
2-[4-(3,5-dimethyl-1H-pyrazol-4-yl)-phenyl]-2-phenyl-ethylamine;  
2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethylamine;  
2-[3-(3,5-dimethyl-1H-pyrazol-4-yl)-phenyl]-1-phenyl-ethylamine;

- 3-phenyl-2-[3-(1H-pyrazol-4-yl)-phenyl]-propylamine;  
 3-phenyl-2-[4-(1H-pyrazol-4-yl)-phenyl]-propylamine;  
 {3-(4-chloro-phenyl)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propyl}-methyl-amine;  
 {3-(3,4-difluoro-phenyl)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propyl}-methyl-amine;  
 5 {3-(3-chloro-phenyl)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propyl}-methyl-amine;  
 3-(4-chloro-phenyl)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propionamide;  
 3-(4-chloro-phenyl)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propylamine;  
 3-(3,4-dichloro-phenyl)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propylamine;  
 4-(4-chloro-phenyl)-4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidine;  
 10 4-(4-methoxy-phenyl)-4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidine;  
 4-(4-chloro-phenyl)-1-methyl-4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidine;  
 4-phenyl-4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidine;  
 4-[4-(3,5-dimethyl-1H-pyrazol-4-yl)-phenyl]-4-phenyl-piperidine;  
 dimethyl-{3-[4-(1H-pyrazol-4-yl)-phenyl]-3-pyridin-2-yl-propyl}-amine;  
 15 {2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-dimethyl-amine;  
 {2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-methyl-amine;  
 {2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-methyl-amine (R);  
 {2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-methyl-amine (S);  
 4-{2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-morpholine;  
 20 4-{4-[1-(4-chloro-phenyl)-2-pyrrolidin-1-yl-ethyl]-phenyl}-1H-pyrazole;  
 {2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-isopropyl-amine;  
 dimethyl-{2-phenyl-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-amine;  
 {2,2-bis-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-dimethyl-amine;  
 {2,2-bis-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-methyl-amine;  
 25 2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethylamine (R);  
 2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethylamine (S);  
 2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-acetamide;  
 1-{2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-piperazine;  
 1-{2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-piperidine;  
 30 4-{4-[2-azetidin-1-yl-1-(4-chloro-phenyl)-ethyl]-phenyl}-1H-pyrazole;

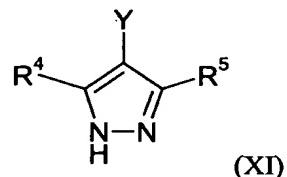
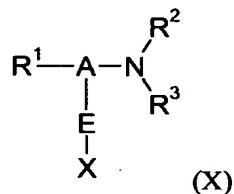
- 1-phenyl-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethylamine;  
 2-(4-chloro-phenyl)-N-methyl-2-[4-(1H-pyrazol-4-yl)-phenyl]-acetamide;  
 N-methyl-2,2-bis-[4-(1H-pyrazol-4-yl)-phenyl]-acetamide;  
 {2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-methyl-amine;  
 5 {2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-ethyl-amine;  
 4-{4-[1-(4-chloro-phenyl)-2-imidazol-1-yl-ethyl]-phenyl}-1H-pyrazole;  
 methyl-{2-(4-phenoxy-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-amine;  
 {2-(4-methoxy-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-methyl-amine;  
 methyl-{2-[4-(pyrazin-2-yloxy)-phenyl]-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-  
 10 amine;  
 methyl-{2-phenoxy-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-amine;  
 2-((4-chloro-phenyl)-[4-(1H-pyrazol-4-yl)-phenyl]-methoxy)-ethylamine;  
 4-{4-[1-(4-chloro-phenyl)-3-pyrrolidin-1-yl-propyl]-phenyl}-1H-pyrazole;  
 4-{4-[3-azetidin-1-yl-1-(4-chloro-phenyl)-propyl]-phenyl}-1H-pyrazole;  
 15 methyl-{3-naphthalen-2-yl-3-[4-(1H-pyrazol-4-yl)-phenyl]-propyl}-amine;  
 {3-(4-fluoro-phenyl)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propyl}-methyl-amine;  
 4-{4-[4-(4-chloro-phenyl)-piperidin-4-yl]-phenyl}-1H-pyrazole-3-carbonitrile;  
 3-(4-phenoxy-phenyl)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propylamine;  
 1-{(4-chloro-phenyl)-[4-(1H-pyrazol-4-yl)-phenyl]-methyl}-piperazine;  
 20 1-methyl-4-{phenyl-[4-(1H-pyrazol-4-yl)-phenyl]-methyl}-[1,4]diazepane;  
 {3-(3-chloro-phenoxy)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propyl}-methyl-amine;  
 methyl-{2-phenyl-2-[6-(1H-pyrazol-4-yl)-pyridin-3-yl]-ethyl}-amine;  
 4-{4-[1-(4-chloro-phenyl)-3-imidazol-1-yl-propyl]-phenyl}-1H-pyrazole;  
 4-[4-(3-imidazol-1-yl-1-phenoxy-propyl)-phenyl]-1H-pyrazole;  
 25 4-{4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidin-4-yl}-phenol;  
 1-{(4-chloro-phenyl)-[4-(1H-pyrazol-4-yl)-phenyl]-methyl}-piperazine;  
 {2-(4-fluoro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-methyl-amine;  
 {2-(3-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-methyl-amine;  
 4-[4-(2-methoxy-ethoxy)-phenyl]-4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidine;  
 30 4-[4-(3-methoxy-propoxy)-phenyl]-4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidine;

- 3-(3,4-dichloro-phenyl)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propionamide;  
 2-(4-{2-methylamino-1-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-phenoxy)-  
 isonicotinamide;  
 {2-(3-chloro-phenoxy)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-methyl-amine;  
 5      3-{2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethylamino}-propan-1-ol;  
 2-{2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethylamino}-ethanol;  
 3-{2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethylamino}-propan-1-ol;  
 2-{2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethylamino}-ethanol;  
 {2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-cyclopropylmethyl-  
 10     amine;  
 methyl-[2-[4-(1H-pyrazol-4-yl)-phenyl]-2-(4-pyridin-3-yl-phenyl)-ethyl]-amine;  
 4-{3-methylamino-1-[4-(1H-pyrazol-4-yl)-phenyl]-propyl}-phenol;  
 3-(4-methoxy-phenyl)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propylamine;  
 4-(4-chloro-phenyl)-4-[4-(3-methyl-1H-pyrazol-4-yl)-phenyl]-piperidine;  
 15     2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-morpholine;  
 (4-{4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidin-4-yl}-phenoxy)-acetic acid;  
 4-{4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidin-4-yl}-benzonitrile;  
 {2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-propyl}-methyl-amine;  
 1-(4-chloro-phenyl)-2-methylamino-1-[4-(1H-pyrazol-4-yl)-phenyl]-ethanol;  
 20     2-amino-1-(4-chloro-phenyl)-1-[4-(1H-pyrazol-4-yl)-phenyl]-ethanol;  
 4-(3,4-dichloro-phenyl)-4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidine;  
 4-(3-chloro-4-methoxy-phenyl)-4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidine;  
 4-(4-chloro-3-fluoro-phenyl)-4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidine;  
 4-[4-(1H-pyrazol-4-yl)-phenyl]-1,2,3,4,5,6-hexahydro-[4,4']bipyridinyl;  
 25     3-(3-chloro-phenyl)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propylamine;  
 2-methylamino-1-(4-nitro-phenyl)-1-[4-(1H-pyrazol-4-yl)-phenyl]-ethanol;  
 2-(3-chloro-4-methoxy-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethylamine;  
 2-(4-chloro-phenyl)-2-fluoro-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethylamine;  
 3-(3,4-dichloro-phenyl)-3-[6-(1H-pyrazol-4-yl)-pyridin-3-yl]-propylamine;  
 30     2-(4-chloro-3-fluoro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethylamine;

- 4-(2-chloro-3-fluoro-phenyl)-4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidine;  
1-{(3,4-dichloro-phenyl)-[4-(1H-pyrazol-4-yl)-phenyl]-methyl}-piperazine;  
2-(3,4-dichloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethylamine;  
{2-(3-chloro-4-methoxy-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-methyl-  
5 amine;  
4-{4-[2-azetidin-1-yl-1-(4-chloro-phenoxy)-ethyl]-phenyl}-1H-pyrazole;  
3-(3-chloro-4-methoxy-phenyl)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propylamine;  
{3-(3-chloro-4-methoxy-phenyl)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propyl}-methyl-  
amine;  
10 1-{(3,4-dichloro-phenyl)-[4-(1H-pyrazol-4-yl)-phenyl]-methyl}-piperazine; or  
C-(4-chloro-phenyl)-C-[4-(1H-pyrazol-4-yl)-phenyl]-methylamine;  
and salts, solvates, tautomers and N-oxides thereof.
50. A compound according to claim 49 which is 2-amino-1-(4-chloro-phenyl)-1-[4-(1H-pyrazol-4-yl)-phenyl]-ethanol or a salt, solvate, tautomer or N-oxide thereof.
- 15 51. A compound according to any one of the preceding claims in the form of a salt, solvate, ester or N-oxide.
52. A compound as defined in any one of claims 1 to 51 for use in medicine.
53. A compound as defined in any one of claims 1 to 51 for use in (a) the prophylaxis or treatment of a disease state or condition mediated by protein kinase B; or (b) 20 the prophylaxis or treatment of a disease state or condition mediated by protein kinase A.
- 25 54. A compound as defined in any one of claims 1 to 51 for use in the prophylaxis or treatment of a disease state or condition which is selected from a carcinoma of the bladder, breast, colon, kidney, epidermal, liver, lung, oesophagus, gall bladder, ovary, pancreas, stomach, cervix, endometrium, thyroid, prostate, or skin, a hematopoietic tumour of lymphoid lineage, a hematopoietic tumour of myeloid lineage, thyroid follicular cancer, a tumour of mesenchymal origin, a tumour of

the central or peripheral nervous system, melanoma, seminoma, teratocarcinoma, osteosarcoma, xeroderma pigmentosum, keratoctanthoma, thyroid follicular cancer, or Kaposi's sarcoma.

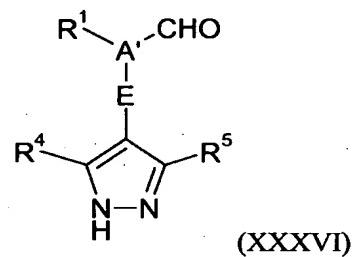
55. A compound as defined in any one of claims 1 to 51 for use in the prophylaxis or treatment of a disease state or condition which is selected from breast cancer, ovarian cancer, colon cancer, prostate cancer, oesophageal cancer, squamous cancer and non-small cell lung carcinomas.
56. The use of a compound as defined in any one of claims 1 to 51 for:
- the manufacture of a medicament for the prophylaxis or treatment of a disease state or condition mediated by protein kinase B; or
  - the manufacture of a medicament for the prophylaxis or treatment of a disease state or condition mediated by protein kinase A; or
  - the manufacture of a medicament for the prophylaxis or treatment of a disease state or condition arising from abnormal cell growth;
  - the manufacture of a medicament for the prophylaxis or treatment of a disease in which there is a disorder of proliferation, apoptosis or differentiation.
57. A pharmaceutical composition comprising a novel compound as defined in any one of claims 1 to 51 and a pharmaceutically acceptable carrier.
58. A process for the preparation of a compound of the formula (I) as defined in any one of claims 1 to 51, which process comprises:
- the reaction of a compound of the formula (X) with a compound of the formula (XI) or an N-protected derivative thereof:



wherein A, E, and R<sup>1</sup> to R<sup>5</sup> are as defined in any one of claims 1 to 51, one of the groups X and Y is selected from chlorine, bromine, iodine and trifluoromethanesulphonate, and the other one of the groups X and Y is a boronate ester or boronic acid residue, in the presence of a palladium catalyst and a base;

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- (b) the reductive amination of a compound of the formula (XXXVI):



with HNR<sup>2</sup>R<sup>3</sup> in the presence of a reducing agent; and optionally

- (c) the conversion of one compound of the formula (I) into another compound of the formula (I).

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